MAGNETIC NANOPARTICLES IN MAGNETIC FLUIDS

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ABSTRACT

Magnetic fluids are stable colloidal systems of fine single-domain magnetic particles (for example Fe_3O_4, γ-Fe_2O_3, Co, $MnFe_2O_4$, etc.) that are suspended in liquid carrier such as water, mineral oil, damping oil, paraffin, kerosene and so on. The properties of magnetic fluids are well controlled by external magnetic field that gives broad possibilities for technical and biomedical applications. In this contribution we want to discuss briefly history of magnetic fluids, the role of magnetic particles in magnetic fluids, their basic properties and some technical and biomedical applications. In detail some of the main results of magnetic fluids for power transformers, composite systems of liquid crystal and magnetic particles and magnetic fluid for drug targetingare presented.

Keywords: *magnetic fluid, magnetic nanoparticles, transformers, ferronematics, drug targeting*

1. INTRODUCTION

Magnetic nanoparticles play very important role in magnetic fluids which are probably first prepared nano-object in the history of nano-area. Magnetic fluids have existed in one form or another for over 200 years. Although intensive research on magnetic fluids did not start until the 1960, the preparation of water based magnetic fluids had already been described in 1938 by Elmore [1]. The first ferrofluids were primary used as a means to study magnetic domain structure in solids. The modern era of ferrofluids manufacture begins when ferrofluids were made using colloidally stable particles using the co-precipitation technique [2,3]. This technique is still used today as a basis for producting high quality colloid suspensions of magnetic particles in a variety of liquid carrier fluids.

The most commonly used ferrofluid contains spherical magnetic particles with typical size of 10 nm, dispersed in an apolar solvent. Sedimentation of these particles is sufficiently counteracted by Brownian motion to keep them dispersed for years. To prevent aggregation, the colloids can be covered with a thin layer of surfactant, commonly a monolayer of oleic acid (steric repulsion), or the particles are prevented from sticking to each other by electrostatic bilayer (electrostatic repulsion), which makes the particles stable in many liquid carriers. The behaviour of such ferrofluids is mainly determined by their magnetic properties. Because of their small size, these magnetic colloids contain a single magnetic domain, and therefore have a permanent magnetic moment proportional to their volume. Although magnetic colloids are ferromagnetic on the molecular scale, they resemble a paramagnet on the colloidal scale. Such a system of particles does not retain any remanent magnetisation as it is superparamagnetic, i.e. the particles have no hysteresis. Due to their superparamagnetic nature, ferrofluids behave as non-magnetic fluids under conditions of zero magnetic field. Each coated particle will behave as a single domain particle and so any rotation of magnetisation is brought about both Brownian and Néel mechanisms. Thermal fluctuation are sufficient to keep the magnetisation vector of particles randomly oriented, such that the net magnetisation of the system is zero. In the presence of a magnetic field, the magnetic moment of the particles will try to align with the magnetic field direction leading to a macroscopic megnetization of the liquid. An important property of concentrated ferrofluids is that they are strongly attracted by permanent magnets, while their liquid character is preserved. The attraction can be strong enough to overcome the force of gravity.

The magnetic control of ferrofluids forced strong efforts in the desing of applications using the influence of a magnetic field, in particular the possibility to position the fluid inside a technical device, leading to lot of application for ferrofluids [4]. Some of these reached commercial importance and are widely used in everyday life. Ferrofluids are widely used as lubricating, airtight seals in rotary shafts. A magnetic field gradient keeps the ferrofluids in place, even in case of pressure differences between the two separated compartments. Today, many computer hard disk drives contain a ferrofluid-sealed shaft. Ferrofluids are also used to improve heat dissipation in loudspeaker coils, enabling higher output power. When non-magnetic objects are immersed in a ferrofluid and subjected to the field gradient of permanent magnet, the object will be effectively repelled by magnet (actually, the ferrofluid is atracted and drives away the object). When combined with a gravitational or centrifugational force opposing the effective magnetic force, this effective repulsion has the same effect as a density gradient of solvent. This principle is used to separate materials into density fractions, for instance in the mining industry or waste processing [5]. Because the effective density of ferrofluids can be much higher than that of ordinary liquids, density-based separation with ferrofluids can be much higher than that of ordinary liquids. Density-based separation with ferrofluids is also suitable for high density materials such as nonmagnetic metals, diamonds, etc.

Magnetic nanoparticles offer some attractive possibilities in biomedicine as they have controllable sizes ranging from a few nanometers up to tens of nanometers,

which places them at dimensions that are smaller than or comparable to those of the cell (10-100 μm), a virus (20-450 nm), a protein (5-50 nm) or a gene (2 nm wide and 10-100 nm long). This means that they can get close to a biological entity of interest. Indeed, they can be coated with biological molecules to make them interact with or bind to a biological entity, thereby providing a controllable means of tagging or addressing it.

The major disadvantage of most chemoterapies is that they are relatively non-specific. The therapeutic drugs are administered intravenously leading to general systemic distribution, resulting in deleterious side-effects as the drug attacts normal, healthy cells in addition to the target tummour cells. However, if such treatments could be localized, e.g. to the site of a joint, then the continued use of these very potent and effective agents could be made possible. Recognition of this led researchers to propose the use of magnetic carriers to target specific sites (generally cancerous tummours) within the body. In magnetically targeted therapy, a cytotoxic drug is attached to a biocompatible magnetic nanoparticle carrier. Generally, the magnetic component of the particle is coated by a biocompatible polymer such as PEG, PLA or dextran, although recently inoganic coatings such as silica have been developed. The coating acts to shield the magnetic particle from the surrouding environment and can also be functionalized by attaching carboxyl groups, biotin, avidin, carbodi-imide and other molekules. These molecules then act as attachment points for the coupling of cytotoxic drugs or target antibodies to the carrier complex. The carriers typically have one of two structural configurations: a magnetic particle core coated with biocompatible polymer or porous biocompatible polymer in which magnetic nanopartiles are precipitated inside the pores. The physical and chemical properties of magnetic fluids are strongly influenced by details of the size distribution of dispersed colloidal magnetic particles.

The magnetic nanoparticles can be made to resonantly respond to a time-varying magnetic field, with advantageous results related to the transfer of energy from exciting field to nanoparticles. For example, the particles can be made to heat up, which leads to their use as hypertermia agents. Hypertermia is a therapeutic procedure used to rice the temperature of a region of the body affected by malignancy or other growths. The rationale is based on a direct cell-killing effect at temperature above 41-42°C. Modern clinical hypertermia trials focus mainly on the optimization of thermal homogenity at moderate temperatures (42-43°C) in the target volume. The temperature increase required for hyperthermia can be achieved also by using fine iron oxide magnetic particles. The physical principle for which a magnetic material can be heated by action of an external alternating magnetic field are the loss processes that occur during the reorientation of magnetization of magnetic materials with low electrical conductivity. The advantage of magnetic hyperthermia is that allows the heating to be restricted to the tumour area. Magnetic separation has been succesfully applied to many aspects of biomedical and biological research. In this procedure the magnetic adsorbent is added to a solution or suspension containing the target. This is adsorbed onto the magnetic adsorbent and then the adsorbent with adsorbed target is recovered from the suspension using an appropriate magnetic separator [6]. Magnetic separation has proven to be a highly sensitive technique for the selection of rare tumour cells from blood, and is especially well suited to the separation of low numbers of target cells. This has, for example, led to the enhanced detection of malarial parasites in blood samples either by utilizing the magnetic properties of the parasite or through labelling the red blood cells with an immunospecific magnetic fluid. These, and many other potential applications, are made avaliable in biomedicine as a result of the special physical properties of magnetic nanoparticles.

2. METHODS

In this contribution three main results in the following areas are presented:

(i) the DC and AC dielectric breakdown strength of magnetic fluids based on transformer oil TECHNOL US 4000, with different saturation magnetizations, investigated in various orientations of external magnetic field. As a boundary volume concentration of magnetic particles, below which the magnetic fluids have better or not worse dielectric properties than pure transformer oil, the volume concentration Φ=0.01 was found. Thus magnetic fluids with Φ<0.01 are suitable for the use as a high-voltage insulation [7].

(ii) the structural changes in ferronematic samples based on the thermotropic nematic 4-(trans-4'-n-hexylcyclohexyl)-isothiocyanatobenzene (6CHBT). The nematic 6CHBT was doped with a magnetic suspension consisting of magnetite particles of different shape. Due to the small volume concentrations of the magnetic particles ($2x10^{-4}$) and surfactant in the prepared ferronematic samples the interparticle dipole-dipole interactions are avoided. The structural transitions in ferronematic samples were indicated by capacitance measurements [8].

(iii) the preparation of magnetic fluid for drug targeting. One of the prerequisites for success of the application of drug targeting for treatment of localised diseases is development of an effective method to transport the drug to the target site in organism. In recent years, there has been growing interest in magnetic substances for the creation of magnetic pharmaceutical preparations. In particular, magnetite can be used as a drug carier, which makes it possible to create magnetically guided drugs. Such drugs can be delivered to a target organ under the action of an external magnetic field [9].

RESULTS

2.1. Dielectric breakdown

The insulation fluids in power transformers perform two main functions – insulating and cooling. The highly refined mineral oils (transformers oils), typically used as insulating fluids, have low thermal conductivity and thus perform low-efficiency cooling. It has been shown that the heat transfer in electromagnetic devices can be substantially improved by using magnetic fluids consisting of nanosized magnetic particles suspended in transformer oil. The presence of foreign particles in liquid insulators has a profound effect on their dielectric

breakdown strength. The magnetic (e.g. magnetite Fe_3O_4) particles are polarisable and are of higher permittivity than the surrounding liquid. As a result they experience an electrical force directed towards the place of maximum stress. With uniform field electrodes the movement of particles is presumed to be initiated by the surface irregularities on the electrodes, which give rise to local field gradients. The accumulation of particles continues and tends to form a bridge across the gap, what leads to the breakdown initiation. Due to the magnetic dipole-dipole interaction between the particles, the chains and chain like elongated clusters are formed, what results in magnetomechanical and magnetooptical effects, magneto-dielectric behaviour etc. The aggregation of magnetite particles in magnetic field produced by the transformer windings influences the magneto-dielectric behaviour and the dielectric breakdown strength of a transformer oil based magnetic fluid.

The measured DC and AC dielectric breakdown strengths of magnetic fluid, compared with the DC and AC dielectric breakdown strengths of pure transformer oil, are shown in Figure 1.

While the DC dielectric breakdown strength of studied magnetic fluid was found to be higher than that of pure transformer oil, the AC breakdown strength remains comparable with that of transformer oil, but not worse.

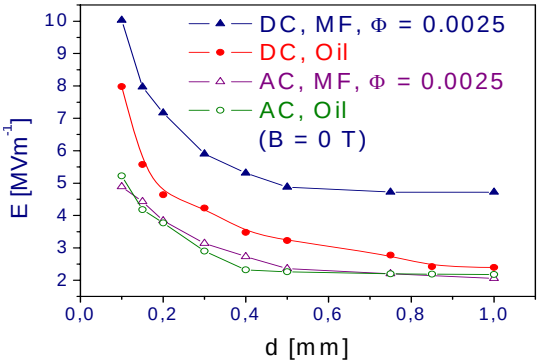

Fig. 1 The DC and AC dielectric breakdown strengths of magnetic fluid ($\Phi = 0.0025$) and pure transformer oil

2.2. Structural changes in ferronematics

Ferronematics are complex colloids based on a liquid crystal matrix doped with fine magnetic particles and were first suggested on theoretical grounds in 1970 by Brochard and de Gennes [10]. The surface anchoring in the magnetic particles couples the magnetic and nematic order and increases the weak magnetic interaction. This gives the better possibility to control behaviour of liquid crystals in external magnetic field. The observations of the structural transitions in ferronematics in external field can be used for determination of the type of anchoring of nematic molecules on magnetic particle surfaces as well as the surface density of the anchoring energy W at the nematic- magnetic particle boundary. The obtained values of the critical magnetic fields for different bias voltages are summarized in Fig. 2, that shows dependence of critical magnetic field on the applied bias voltage for pure 6CHBT and 6CHBT doped with spherical, chain-like and rod-like magnetic particles. This figure demonstrate that the shape of magnetic particles has significant influence on the sensitivity of ferronematics on the applied magnetic field.

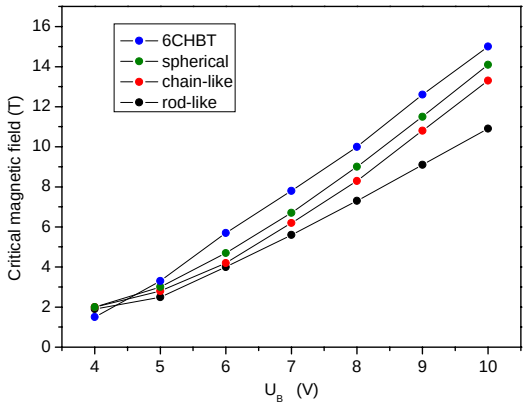

Fig. 2 Dependence of critical magnetic field on applied voltage for pure 6CHBT and 6CHBT doped with magnetic particles of different shape

2.3. Magnetic nanoparticles for drug targeting delivery

For biomedical application the magnetic particles were coated with sodium natrium as a first surfactant and polyethylene glycol (PEG) as a second surfactant to improve their biocompatibility. Prepared biocompatibile magnetic fluid and anticancer drug Taxol were incorporated to the PLGA nanospheres. As prepared samples were used in *in vitro* and *in vivo* experiments. The *in vitro* release profiles of Taxol from the magnetic nanosphers were examined in two groups of aqueous media: (1) 0.2M phosphate buffer of pH = 6.0, 6.6 and 7.4 and (2) 0.2M phosphate buffer containing sodium salicylate, as a hydrotropic agent, with various molar concentrations (1M, 2M and 3M) of pH = 6.0, 6.6 and 7.4.

Table 1 Summarized results of particle size (PCCS, SEM), colloidal stability (critical aggregation concentration, CAC) and toxicity (LD_{50})

Sample	*Particle size [nm]*		*CAC [mol/dm³ NaCl]*	*LD_{50}*
	PCCS (median)	SEM	PCCS Turbidimetry	
MFPEG	65	60	0.095 0.095	400 mg Fe_3O_4/kg
NPs (without MF/TAX)	195	198	1.6 1.45	221 mg PLGA/kg
TAXNPs (without MF)	204	208	1.2 1.2	226 mg PLGA/kg (at 11.3 mg TAX/kg)
MNPs (without TAX)	230	224	stable stable	174 - 198 mg PLGA/kg
TAXMNPs	232	240	stable stable	> 154 mg PLGA/kg (at 7.7 mg TAX/kg)

In vivo toxicity of PLGA composite NPs and magnetic fluid (as a blank) was evaluated in ICR mice after intravenous administration using the preliminary 'up & down' method (OECD 421). The LD_{50} value of magnetic fluid MFPEG (conc. 0.1 g Fe_3O_4/1 ml) determined in male mice was 400 mg Fe_3O_4/kg. The LD_{50} value of PLGA NPs

(conc. 10 mg PLGA/1 ml) determined in male mice was 221 mg PLGA/kg. For the formulation of MNPs without TAX (100 mg PLGA/50 mg Fe_3O_4/10 ml) the PLGA was assumed to be the limit component and for this reason the LD_{50} is expressed in the concentration of this component. LD_{50} was determined to be in the range of 174–198 mg/kg; doses of 174 and 198 were applied three times because the dose 174 mg/kg was not lethal for any of the animals, the dose of 198 mg/kg caused the death of all of the animals. The last experiment was done with TAXMNPs (100 mg PLGA/50 mg Fe_3O_4/5 mg TAX). The dose of 154 mg PLGA/kg had not been lethal. The results are summarized in Table 1.

3. CONCLUSIONS

To conclude it can be said that the field induced aggregation of magnetic particles can significantly change the dielectric breakdown strength of magnetic fluids if the sizes of the aggregates are comparable with the distance between the electrodes of the measured gap. Regarding to the better heat transfer, provided by magnetic fluids, their application in power transformers may lead to the improvement of the operation of these devices.

Doping with magnetic particles shaped similarly to the liquid crystal molecules, gives better exploration of ferronematics in the applications where the magnetic field is necessary to control the orientation of the liquid crystal molecules. The magnetic nanoparticles together with anticancer drug taxol encapsulated into the polymer nanospheres of spherical shape of mean diameter aproximately 250 nm, which is a relevant size for intravenous administration were prepared and characterized. The functionalised spheres have 5-times lower toxicity in comparison with pure taxol and are suitable for magnetic drug targeting.

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